M.L.

Hypersplenism and Surgery of the Spleen

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Based on Exhibits presented at the Annual Meetings in 1947 and 1951 of the American Medical Association Recipients in 1951 of the A.M.A. Silver Medal.



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PREFACE

The spleen remains an organ of mystery. It seems to be a part of the endocrine system, but of this, real proof is lacking. It may be removed from the body with impunity, but it has many subtle functions, connected chiefly with the bone marrow. Every so often, particularly when enlarged, it seems to bring about serious blood dyscrasias, and its removal may then become essential. "Hypersplenism" may not be as exact a term as hyperthyroidism, but it is useful in describing certain blood cytopenias, usually with splenomegaly. Surgery of the spleen has become bolder in recent years, and has extended into the field of the leukemias and into shunting blood from a hypertensive portal circulation into the general flow.

This work, an extension of "Spleen and Hypersplenism" by Dameshek and Estren, (1948) has much new material on hemolytic anemia and idiopathic thrombocytopenic purpura, with entirely new sections on methods for splenectomy and the relief of portal hypertension. It came about through presentation of the American Medical Association Exhibit on "Hypersplenism and Surgery of the Spleen" in 1950 which was awarded the Billings Silver medal. We hope that this volume, presented in graphic style, will help to interest and instruct, and perhaps even to spark further investigation into splenic functions and dysfunctions.

CONTENTS

FACTS THE SPLEEN FANCIES

GALEN SAID (150 A.D.):

"The spleen is an organ full of mystery"

SUPERSTITIONS:

It is the site of bad humors
"To vent one's spleen." "Spleeny"
Removal of spleen helps runner's wind
Removal is incompatible with life
Removal leads to death in 7 years

FACTS:

Spleen has many functions,
although not essential to life

CHIEF IMPORTANCE:

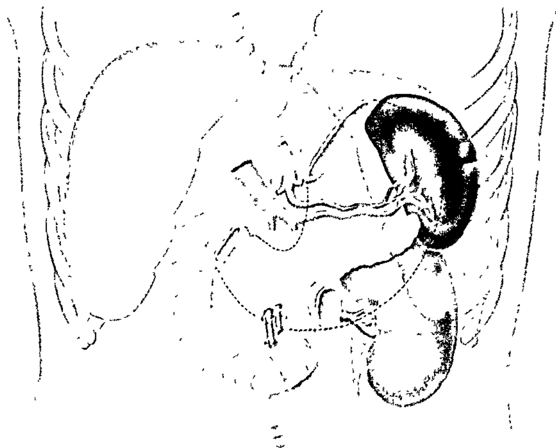
Spleen may develop abnormal functions,
jeopardize life, and require removal

PURPOSE OF THIS STUDY:

1. Recognition and understanding of splenic dysfunctions, in particular Hypersplenism
2. Description of appropriate therapy, in particular the surgical techniques.

ANATOMY

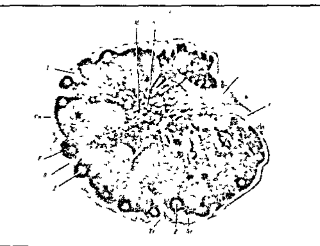
The spleen is a large organ, weighing 100-150 grams
An enormous lymph node between an artery and vein
Blood supply very rich, suggesting functional importance
Splenic artery is the largest branch of the coeliac axis
Splenic vein is the largest tributary of the portal vein



Spleen borders diaphragm, stomach, pancreas and kidney
Not normally palpable, it can be percussed
Splenic palpation is often neglected;
carefully done, it is often rewarding

HISTOLOGY

The spleen is a collection of supporting, vascular, hematopoietic and hemolytic tissues

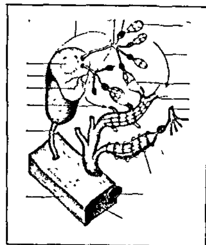


Photomicrograph - Low Power

1. SUPPORTING CONNECTIVE TISSUE
   - Capsule
   - Trabeculae
   - Reticulum
2. VASCULAR SYSTEM
3. WHITE PULP
   - Malpighian bodies, lymphoid tissue
4. RED PULP
   - Reticular fibers
   - Reticulo-endothelial cells
   - Blood cells

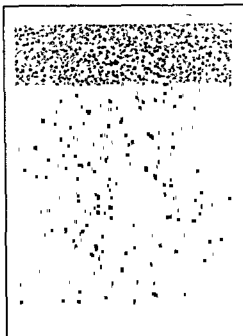
VASCULAR SYSTEM

Coeliac Axis ⟶ Splenic Artery
Trabecular Artery
Follicular (Central) Artery
Pulp (Penicilliary) Artery
Venous Sinusoids
Pulp Veins
Trabecular Vein
Splenic Vein
Portal Vein



Splenic Circulation
Schematic

HISTOLOGY



Malpighian Follicle

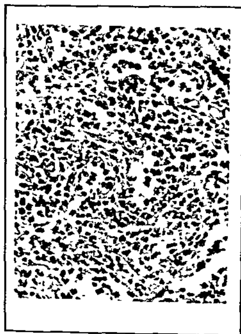
"WHITE" PULP

Mostly lymphatic tissue which surrounds splenic arterioles to form Malpighian or splenic follicles.

"RED" PULP

A conglomeration of cells between terminal blood vessels and follicles

- Reticulum fibers
- Lymphocytes
- Reticulo-endothelial cells
- Cells from circulating blood
  - Erythrocytes
  - Leukocytes
  - Platelets



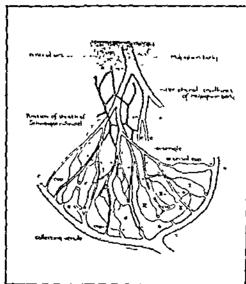
Splenic Pulp (Red Pulp)

HISTOLOGY

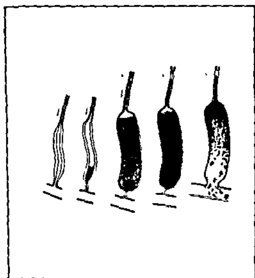
VASCULAR "BIO"-HISTOLOGY (KNISELY)

Much controversy has
taken place *re*
"Open" vs "Closed" circulation

Knisely's studies on intact
Animals showed a closed
system with valves in
sinusoids
However, other similar studies
have demonstrated open system



"Closed" system of blood flow
through spleen (Knisely)



Empty & Full Sinuses:
Erythrostasis (Knisely)

Blood flow very sluggish
Erythrostasis in closed sinuses
May go on for hours

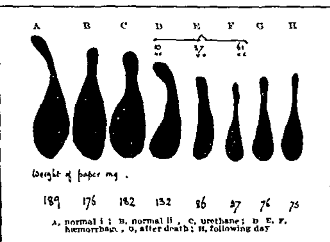
Does spleen do something to blood?

Possibilities: Mechanical (stasis)
Chemical (Lysolecithin)
Humoral

PHYSIOLOGY

RESERVOIR FUNCTION AND ERYTHROSTASIS

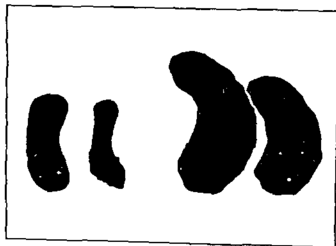
Spleen under control of autonomic nervous system. Various stimuli cause contraction and dilatation. Sinusoids may dilate to contain excess blood. Spleen has a "reservoir" function (Barcroft) and stores up to 20% blood volume.



Effect of Hemorrhage (Barcroft)

Barcroft showed that hemorrhage, excitement, exercise, and anoxia caused contraction.
Splenic contraction in emergency → "Auto-transfusion"

Spleen is also like a warm test-tube containing static blood. Erythrostasis results in increased thickness of red cells.
The oldest red cells (Spherocytes) are the most vulnerable to destruction.



Effects of exercise and excitement (Barcroft)

PHYSIOLOGY

PRODUCTION AND DESTRUCTION OF BLOOD CELLS

PRODUCTION

In the embryo, all blood elements produced in spleen
In adult, only lymphocytes and monocytes produced
Contains largest unit of reticulo-endothelial cells
These have many functions and are "pluripotential"
They have many latent blood-forming qualities
Under stress, bone-marrow elements are produced
I.E. Extra-medullary hematopoiesis or myeloid metaplasia
Blood shows nucleated red cells & early granulocytes
(Lack of normal splenic regulation; inefficient blood production)

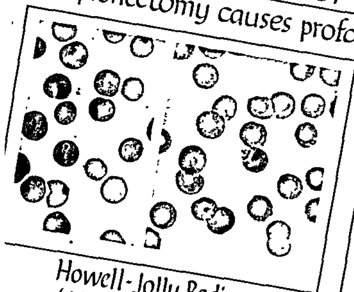
DESTRUCTION

Red Cells: Spleen the "graveyard" of the red cell
not its "slaughter house"
Actual means of destruction unknown
Red cells made thicker by erythrostasis
Thick red cells vulnerable
R-E cells convert hemoglobin to bilirubin
White Cells: Destroyed here (?) No real evidence
Platelets: Destroyed here (?) No real evidence

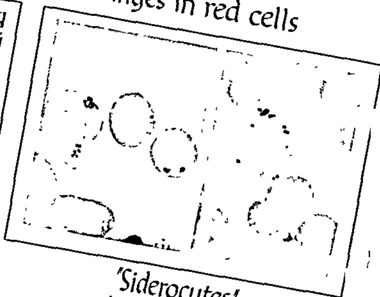
PHYSIOLOGY

EFFECTS OF SPLENECTOMY

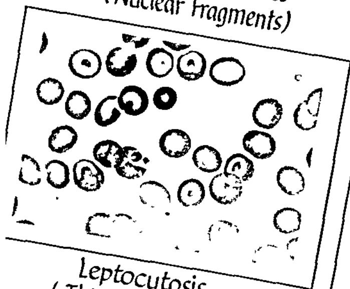
Splenectomy causes profound changes in red cells



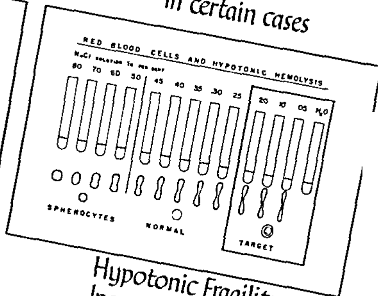
Howell-Jolly Bodies
(Nuclear Fragments)



'Siderocytes'
in certain cases



Leptocytosis
(Thin Target Cells)



Hypotonic Fragility
Increased Resistance

Following splenectomy, red cell destruction diminishes
Without splenectomy similar changes suggest
splenic atrophy and Hyposplenism

PHYSIOLOGY

EFFECTS OF SPLENECTOMY

A good way to study an organ's function is to note effects of its removal
Splenectomy causes many changes in the blood cells:

BLOOD COUNTS

	Splenectomy Before	Splenectomy After
RBC ↑	5.0 M	5.5 M
WBC ↑	7000	15000
Platelets ↑	400,000	1,000,000

CONCLUSIONS: Spleen controls to some extent the growth and emission of the bone marrow blood cells

RED CELLS

1. Target cells (Leptocytes) thin
   Increased hypotonic resistance
2. Howell-Jolly bodies
   Occasional nucleated red cells
3. Diminished red cell destruction
   Hemolytic index diminished

Spleen makes red cells thicker
Controls their denucleation
May modify their life span
Partakes in hemoglobin destruction

WHITE CELLS

	Splenectomy Before	Splenectomy After
WBC ↑	7000	15000
Polys. ↑ or same	70% 5000	50-60% 7500-9000
Lymphs. ↑	20% 1400	40-50% 6000-7000

Spleen regulates
Granulocytopoiesis
and
Lymphocytopoiesis

PLATELETS

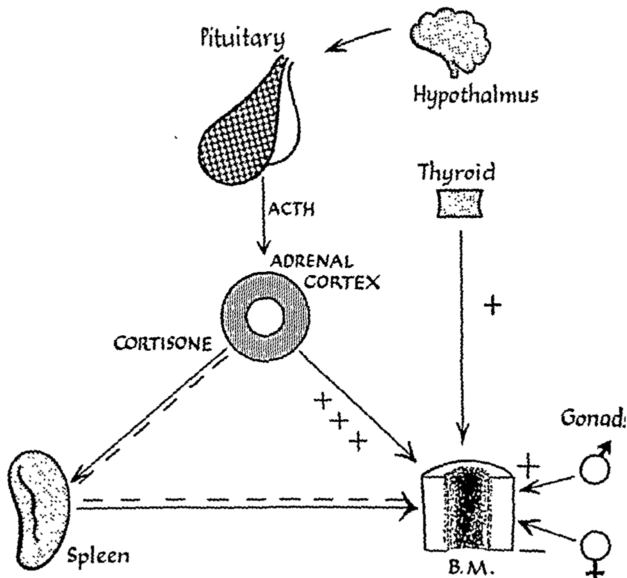
	Before	After
Plts. ↑	400,000	1,000,000

Spleen controls or regulates platelet production by megakaryocytes

GENERAL CONCLUSION: Spleen probably produces humoral factors acting upon bone marrow and lymphoid tissue

THE SPLEEN AND BONE MARROW IN THE ENDOCRINE SYSTEM

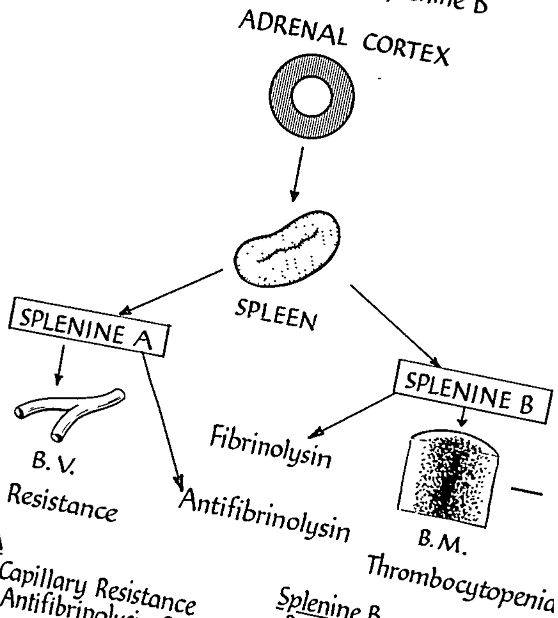
ADRENAL CORTEX — BONE MARROW — SPLENIC AXIS



Adrenal Cortex: Stimulates Bone Marrow
: Inhibits Spleen and Lymphoid Tissue
: Inhibits Bone Marrow

SPLEEN AND SPLENIC HORMONES

G. Ungar: Spleen produces two antagonistic hormones:
Splenine A and Splenine B

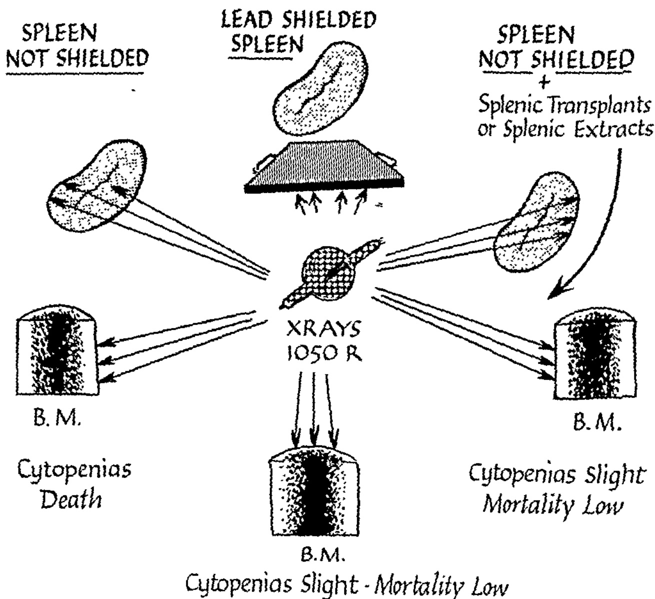


Splenine A
Increases Capillary Resistance
Enhances Antifibrinolysin Production

Splenine B
Produces Thrombocytopenia
Increases Fibrinolysin

SPLEEN AND SPLENIC HORMONES

L.M. Jacobson:
Xray destruction of bone marrow in rats prevented by Spleen shielding



CONCLUSIONS:

1. Spleen shielding prevents bone marrow injury
2. Spleen contains a humoral factor protecting bone marrow.

PHYSIOLOGY

OTHER METHODS OF STUDY

SPLENIC EXTRACTS

1. Normal: No definite effects
2. From Splenic Thrombocytopenia: *Inconstant thrombocytopenia*
3. From Splenic Neutropenia: Inconstant neutropenic effects.

PARABIOSIS



Physical partnership of two rats
Two circulations become united
Then single or double splenectomies performed

1. Normal spleen of one animal inhibits latent Bartonella infection in both rats (Lauda & Flaum)
2. Spleen regulates red cell denucleation (Hirschfeld, Lauda & Flaum)

PRODUCTION OF SPLENOMEGALY

Congestion of spleen by splenic vein ligation
Splenomegaly & Pancytopenia (Bock & Fraenzel; Jombres)

STUDY OF ABNORMAL SPLENIC CONDITIONS

The body sets up physiopathologic 'experiments.'
Study of cases with splenomegaly & results of splenectomy often lights up certain functions of the spleen

TWO SCHOOLS OF THOUGHT HAVE EMERGED

1. Sequestration - Phagocytosis (Kaznelson, Doan & Wiseman)
2. Marrow inhibition by hormonal regulation (Isaac, Engelbreth-Holm, Dameshek)

PHYSIOLOGY

SUMMARY OF SPLENIC FUNCTIONS

A. Reservoir

B. Organ of Erythrostasis

C. Lymphoid Organ

1. Filter in blood stream
2. Production of Lymphocytes
   - Immune body production
   - Protein metabolism
   - Reciprocal relationship to Adrenal Cortex
   - Lymphocytic defense in Infections

D. Reticulo-Endothelial Organ

1. Phagocytosis
2. Production of Monocytes
   - Monocytic defense in Infections
3. Immune Body Production
4. Destruction of Erythrocytes
   - Formation of Bilirubin
5. Fat Metabolism
6. Potential Blood Forming Organ

E. [illegible])

1. [illegible]
   - control of denucleation
   - control of thickness
2. Granulocytes - control of emission
3. Platelets - control of formation in megakaryocytes
   - ? control of emission

F. Red Cell Hemoglobin Modific[illegible]

[illegible]

- Makes red cells thicker (Spherocytic) by Erythrostasis
- ? Role of Lysolecithin
- May have other functions, i.e. in Hemoglobin Metabolism

HYPERSPLENISM

Nature often sets up excellent "laboratory" experiments
Splenic abnormality may result in serious blood cell disorders
Analysis of such cases and of effects of splenectomy
has led to concept of hypersplenism

Hypersplenism: Exaggerated (humoral) splenic functions with "selective" or "total" reductions of red cells, leukocytes & platelets (cytopenias)

HISTORICAL

Gretsel	1866	"Splenic Anemia"
Banti	1894	"Splenomegaly with Cirrhosis of Liver"
Rendu & Widal	1899	"Hyperactive" Spleen and Cytopenias
Micheli & Banti	1911	"Hemolytic Splenomegaly" Rx: Splenectomy
Isaac	1912	Splenic Hormonal Inhibition of Marrow
Frank	1916	"Aleukia Splenica"
Morawitz-Eppinger	1919	"Hypersplenism"
Engelbreth-Holm	1938	Splenic Control of Cellular Emission from Marrow
Wiseman & Doan	1939	"Splenic Neutropenia"
Dameshek	1941	"[illegible]" "Total" Types
Doan & Wright	1946	"[illegible]"

SPLENOMEGALY WITH CYTOPENIAS

Working Concept:

Anatomic enlargement of spleen→Physiologic hyperfunction

Fact: Various splenomegalies often accompanied by:

Neutropenia, Anemia, or Thrombocytopenia
or combinations of these including Pancytopenia

Therefore: 1. Cytopenia may be expected with almost any type of splenomega
2. Cytopenia plus splenomegaly does not point
to any specific diagnosis, but to hypersplenism

Terminology:

- Suggest Hypersplenism (Pancytopenia, Neutropenia, etc.) secondary to Gaucher's Splenomegaly" etc..
- Term "Banti's Syndrome" meaningless, connoting merely Cytopenia with Splenomegaly.
- "Felty's Syndrome": Splenic Cytopenia secondary to Splenomegaly of Rheumatoid Arthritis

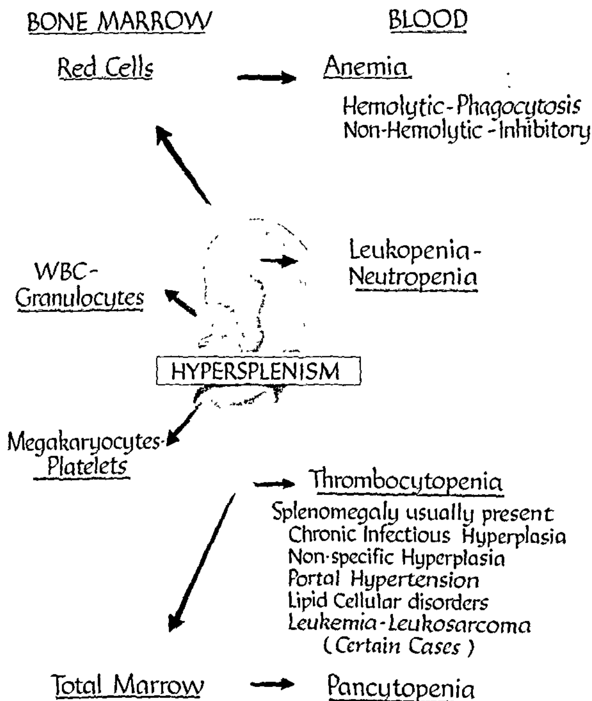
Mechanisms:

Enlarged spleen is hyperactive
Inhibits maturation and/or delivery
of Granulocytes → Neutropenia
of Megakaryocytes →Thrombocytopenia
of Erythrocytes → Anemia
May cause increased hemolysis→Anemia

End Results: -

1. Anemia: Non-hemolytic or Hemolytic
2. Neutropenia (Granulocytopenia)
3. Thrombocytopenia
4. Pancytopenia (Anemia + Neutropenia + Thrombocytopenia

HYPERSPLENIC SYNDROMES



SPLENOMEGALY-KNOWN CAUSE-& HYPERSPLENISM

Cytopenias often accompany diverse types of splenomegaly

ZALMEN K. AGE 5 GAUCHER'S DISEASE PANCYTOPENIA

History: F.H. of splenomegaly
Splenomegaly
Easy bruising

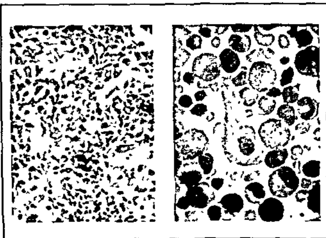
P.E.: Puny boy
Liver 7cm. Spleen enormous
Petechiae Ecchymoses

Blood: Hgb. 9.3 Gm.; RBC 4.07 M.
WBC 2800; P 58% (1600)
Plts. 100,000 (normal 500,000)

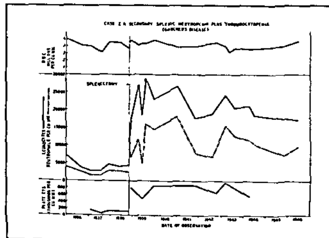
Marrow: Hyperplasia
Gaucher cells

Xrays: "Erlenmeyer Flask" femurs

Splenectomy: 1300 Gm.
Gaucher's Disease



Spleen: Gaucher's disease Marrow: Gaucher cell



Course

DATA: (1) Gaucher's splenomegaly + (2) Cytopenias +
(3) Marrow Hyperplasia + (4) Splenectomy → (5) Normal blood counts /

CONCLUSION:

Gaucher's Splenomegaly → Hypersplenism (Marrow Inhibition)

SPLENOMEGALY-KNOWN CAUSE-& HYPERSPLENISM

Cytopenias occur in various types of portal hypertension with splenomegaly

EVELYN P. AGE 19 CIRRHOSIS OF LIVER PANCYTOPENIA

History: Pain L.U.Q. Epistaxes
Menorrhagia, Easy bruising
Bleeding from gums

P.E.: Pallor
Ecchymoses Petechiae
Splenomegaly 4 f.b.
"Spiders"

Blood: Hgb. 10.1 Gm., RBC 3.63 M
WBC 2300; P 44% (1000)
Plts. 98000
Bilirubin 5 mgs
B.S.P. 18% retention

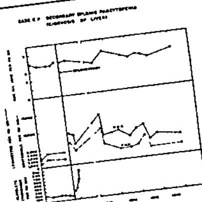
Marrow: Hyperplasia

Xrays: Esophageal varices

Splenectomy: 650 Gm.



Congestive Splenomegaly



Course

DATA: (1) Cirrhosis + (2) Splenomegaly + (3) Cytopenias + (4) Marrow Hyperplasia + (5) Splenectomy → (6) Normal blood counts

CONCLUSIONS:

Congestive Splenomegaly → Hypersplenism (Marrow Inhibition)

Splenectomy relieves hypersplenism but not portal hypertension

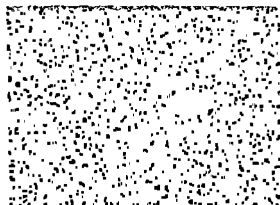
SPLENOMEGALY-KNOWN CAUSE-& HYPERSPLENISM

Cytopenias occur in various subacute and chronic infectious splenomegalies.

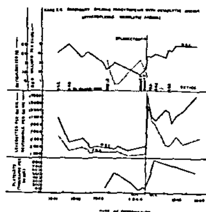
EUGENE R. AGE 67 Tertiary Syphilis Pancytopenia c̄ Hemolytic Anemia

History: 1916-'36 Irregular Rx for syphilis
'40 Hepato-splenomegaly found
'41 Weight loss, slight fever
'44 Increasing pallor
P.E.: Pallor, slight icterus
Liver 8 cm. Spleen 10 cm.

Blood: Hgb. 6.3 Gm.; RBC 1.81 M.
WBC 2500; P. 60% (1500)
Plts. 93,000; Retics. 17%
Bilirubin 3.0 mgs; Serology +++
Marrow: Hyperplasia
Fecal Ubg. 6x normal
Splenectomy: 1650 gms.



Spleen: Non-specific Hyperplasia



Course

DATA: (1) Syphilis → (2) Hepato-Splenomegaly +
(3) Pancytopenia + Increased Hemolysis + (4) Marrow Hyperplasia
+ (5) Splenectomy → (6) Normal Blood counts

CONCLUSION: Chronic Infectious Splenomegaly →
Pancytopenia (Marrow Inhibition plus Hemolysis)

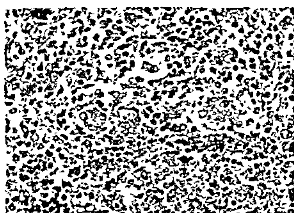
SPLENOMEGALY-KNOWN CAUSE-& HYPERSPLENISM

Splenic cytopenias may occur in malignant splenomegaly including Hodgkin's disease, lymphatic leukemia, lymphosarcoma

ISADORE B. AGE 52 Hodgkin's Splenomegaly. Pancytopenia with Hemolytic

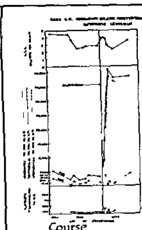
	BEFORE	AFTER
	Splenectomy	
Hgb.	7.3 GM.	10.0 GM.
RBC	2.82 M	3.42 M.
WBC	1,500	7,500
Polys.	700 (47%)	4,900 (65%)
Plts.	167,000	273,000

Fecal Ubg. 3x Normal
Marrow: Hyperplasia of all elements

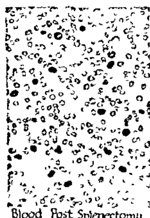


Spleen: 740 Gm. Hodgkin's Disease
Died 5 weeks postoperatively

SIDNEY S. AGE 46 Leukemic Splenomegaly. Pancytopenia



Course



Blood Post Splenectomy

	BEFORE	AFTER
	Splenectomy	
Hgb.	7.8 GM.	8.8 GM.
RBC	2.7 M	3.85 M.
WBC	2,500	40,000
Polys.	1,100 (44%)	4,800 (12%)
Lymphs	1,300 (51%)	34,000 (85%)
Plts.	50,000	100,000

Marrow: Hyperplasia of all elements
Spleen: 1800 GM. Leukemia

Should splenectomy be done in these cases?

1. Individualize each case
2. Hemolysis an indication
3. Splenectomy may improve blood counts
4. Fundamental disease unaltered

SPLENIC NEUTROPENIA

CONCEPT:

Normal spleen regulates granulocyte delivery from marrow
Increased regulatory function → neutropenia
Splenic neutropenia: "Primary" or Secondary

SYMPTOMS: Fatigue, Frequent Infections, Arthralgia

SIGNS: Splenomegaly

LABORATORY: Blood: WBC low; Polymorphs. very low
Bone Marrow: Many granulocytes, normal type
Red Cells & Megakaryocytes normal

DIAGNOSIS: Splenomegaly + Neutropenia + Normal granulocytes in marrow

RULE OUT: Infections: Syphilis, T.B., Malaria, Brucellosis
Malignant Splenomegaly: Hodgkin's, Lymphoma
Leukemia with Splenomegaly
Drug Sensitivity (Agranulocytosis)

RX: Splenectomy
Rationale: Removes Bone Marrow Inhibitor
Pathology: Non-specific Hyperplasia
No Neutro-phagocytosis in Fixed Tissue Sections

SPLENIC NEUTROPENIA-"FELTY'S SYNDROME"

MARGARET C. Age 55 Rheumatoid Arthritis Secondary Splenic Neutropenia

History: Active Rheumatoid Arthritis 1922-'39
Inactive Arthritis since 1939
Mar. '46: severe fatigue
Apr. '46: Infections - gums, mouth, fingers and skin
Fever

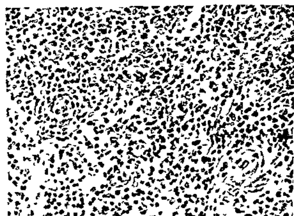
P.E.: Advanced rheumatoid arthritis
Liver 3 f.b. Spleen 4 f.b.
Ulcerations of gums

Blood: Hgb. 11 gms.; RBC 3.95 M.
WBC 1700; P. 18% (300)
Plts. 400,000

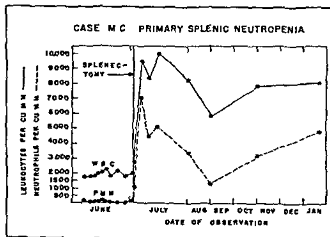
Marrow: Increased granulocytes

Rx.: Penicillin. Pyridoxine, Sulfa. Pentnucleotides. Folic acid. *No Effect*

Splenectomy: 400 gms.



Spleen: Non-Specific Hyperplasia; Vessel lesions



Course

DATA: (1) Rheumatoid arthritis + (2) Splenomegaly
+ (3) Neutropenia + (4) Normal Marrow
+ (5) Splenectomy → Normal WBC

CONCLUSION:

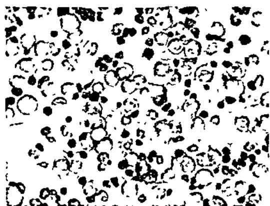
Rheumatoid Splenomegaly → Neutropenia (Marrow Inhibition)

SPLENIC NEUTROPENIA-PRIMARY

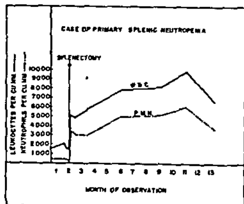
DELORA P. AGE 42 - PRIMARY SPLENIC NEUTROPENIA

History: Apr.'43: Influenza, Pneumonia
Oct.'43: Influenza, Pneumonia
1944: Increasing Fatigue
Vague Joint Pains
P.E.: Thin, sick looking
Slight general lymphadenopathy
Spleen 3 f.b.

Blood: Hgb. 12.5 gm.; RBC 4.2 M.
WBC 1550; P.22% (330)
Plts. 535,000
Marrow: Increased Granulocytes
Lymph node: Nonspecific hyperplasia
Splenectomy: 510 Gm.
Nonspecific hyperplasia



Marrow: Increased Granulocytes



Course

DATA: (1) Idiopathic splenomegaly + (2) Neutropenia +
(3) Marrow Hyperplasia + (4) Splenectomy → (5) Normal Blood counts

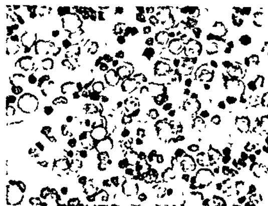
CONCLUSION:
Idiopathic Splenomegaly → Neutropenia (Marrow Inhibition)

SPLENIC NEUTROPENIA-PRIMARY

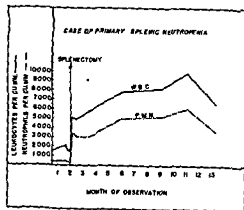
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1944: Increasing Fatigue
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Marrow: Increased Granulocytes
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Nonspecific hyperplasia



Marrow: Increased Granulocytes



Course

DATA: (1) Idiopathic splenomegaly + (2) Neutropenia + (3) Marrow Hyperplasia + (4) Splenectomy → (5) Normal Blood counts

CONCLUSION:

Idiopathic Splenomegaly → Neutropenia (Marrow Inhibition)

SPLENIC NEUTROPENIA + THROMBOCYTOPENIA

Thrombocytopenia may accompany Splenic Neutropenia.
Here, Spleen affects granulocyte delivery and also Platelet Formation/Delivery

GEO. H. AGE 29 Primary Splenic Neutropenia with Thrombocytopenia

Symptoms: Weakness, Arthralgia, Epistaxes
Signs: Splenomegaly 6 F.B.



Marrow shows active granulocytopoiesis.
Increased megakaryocytes; decreased platelet formation

	SPLENECTOMY BEFORE	SPLENECTOMY AFTER
Hgb.	13.3 Gm.	15.2 Gm.
RBC	4.49 M.	4.95 M.
WBC	3,500	10,900
Polys.	2,500	6,500
Plts.	67,000	549,000

Before Splenectomy, Neutropenia and Thrombocytopenia.
After Splenectomy, Normal Blood.
Spleen 1060 Gm.; Fibrosis and Congestion

DATA: (1) Idiopathic Splenomegaly + (2) Neutropenia & Thrombocytopenia + (3) Hyperplastic Marrow + (4) Splenectomy → (5) Normal Blood

CONCLUSION: Idiopathic Splenomegaly → Neutropenia and Thrombocytopenia (Marrow Inhibition)

SPLENIC NEUTROPENIA (PANCYTOPENIA)

AGNES H. AGE 55 Primary Splenic Pancytopenia Marked Neutropenia

History: Aug.'43: Fever. WBC 1500
Nov.'43: Respiratory infection
Dec. '43: Influenza
Jan. '44: Sinusitis
Apr. '44: Herpes Zoster
Nov. '44: Oral Infection
Dec. '44: Conjunctivitis
July '45: Furunculosis
P.E.: Liver 2 F.B. Spleen 4 F.B.

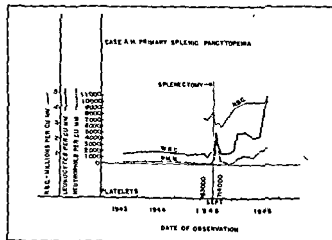
Blood: Hgb. 8.3 gms; RBC 3.4 M
WBC. 1700; P 0-9% (0-200)
Plts. 163,000

Marrow: Increased cellularity
Increased granulocytes

Splenectomy: non-specific hyperplasia
1450 gms.



Marrow: Granulocytic Hyperplasia



Course

DATA: (1) Splenomegaly + (2) Neutropenia + (3) Marrow Hyperplasia + (4) Splenectomy → (5) Normal Blood Counts

CONCLUSION:

Idiopathic Splenomegaly → Pancytopenia with extreme Neutropenia (Marrow Inhibition)

SPLENIC PANCYTOPENIA

Large Hyperactive Spleen Acts on All Three Marrow Elements

[illegible]

Anemia may be Non-Hemolytic (Inhibitory) or Hemolytic (Phagocytic)

NON-HEMOLYTIC	HEMOLYTIC
Neutropenia	Neutropenia
Thrombocytopenia	Thrombocytopenia
Anemia	Anemia
Bilirubin low	Bilirubin normal or high
Reticulocytes low	Reticulocytes high (rarely low)
Fecal Ubg. normal	Fecal Ubg. high

Serum bilirubin may be normal c̄ increased hemolysis
But Fecal urobilinogen always high

The Three Elements in Hypersplenism with Pancytopenia

		WBC Low Polys. Low R.B.C. Low Plts. Low
I. 'Full' Marrow	II. Large Hyperactive Spleen	III. "Depleted" Blood

SPLENIC PANCYTOPENIA

[illegible] Hyperactive Spleen Acts on All Three Marrow Elements
[illegible] nia.

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The Three Elements in Hypersplenism with Pancytopenia

[marrow drawing]	[spleen drawing]	WBC Low Polys. Low R.B.C. Low Plts. Low
I. 'Full' Marrow	II. Large Hyperactive Spleen	III. "Depleted" Blood

PANCYTOPENIA

(Anemia + Leukopenia + Granulocytopenia + Thrombocytopenia)

Normal Blood Count Depends Upon:

I		II		III		IV
Normal Supplies of Iron Liver Folic Acid Vitamin B etc.	+	Normally Functioning Marrow	+	Normal Delivery Mechanism to Blood	+	Normal Removal of Cells from Blood

PANCYTOPENIA MAY BE DUE TO

I. Deficiency of Materials
- Pernicious Anemia & Related Conditions
- Chronic Iron Deficiency
- Vitamin B Complex Deficiency

II. Bone Marrow Disease
- Hypoplasia-Aplasia (Benzol; X-rays & Radioactivity; Idiopathic; Congenital)
- Infiltration (Leukemia; Sarcoma; Myeloma)
- Sclerosis-Fibrosis (Postpolycythemic; others)

III. Impaired Delivery of Cells from Marrow to Blood
- Severe sepsis
- Hypersplenism (Primary & Secondary types)

IV. Increased Removal of Cells from Blood
- Multiple Phagocytosis by Spleen (not observed in our clinic)

SPLENIC PANCYTOPENIA

In Hemolytic cases ("Hypersplenic Hemolytic Anemia")
Hemolysis seems purely Splenic in origin

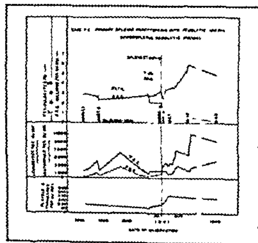
PATSY C. AGE 55 Primary Splenic Pancytopenia, Hemolytic Anemia

History: Relapsing Fever
Increasing fatigue
P.E.: Pallor, slight icterus
Liver 4 f.b.; Spleen 2 f.b.
1941: Increasing pallor
Collapse at work
Downhill course
Increased icterus
Marked Splenomegaly

Blood: Hgb. 7.5 Gm.; RBC 2.58 M.
WBC 1350; P. 46% (620)
Plts. 109,000
Retics 10.2%
Bilirubin 10.6 mgs.
Marrow: Hyperplasia RBC
Normal WBC
Normal Megas.
Fecal Ubg.: 655 mgs.
(8x normal)
Splenectomy: 1000 Gms.
Fibrosis, hemosiderosis

DATA:

(1) Splenomegaly & hepatomegaly +
(2) Pancytopenia with Hemolytic Anemia +
(3) Hyperplastic Marrow +
(4) Splenectomy → (5) Normal blood +
(6) Normal Hemolysis



CONCLUSION:

Idiopathic Splenomegaly → Increased Hemolysis (Phagocytosis) & Cytopenias (Marrow Inhibition)

SPLENIC PANCYTOPENIA

Hypersplenic Hemolytic Anemia May be Associated with Maturation Arrest of Marrow Red Cells (Splenic Inhibition ?)

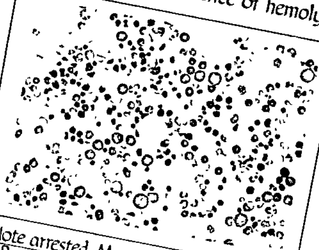
ALICE D. AGE 57 Primary Splenic Pancytopenia, "Occult" Hemolytic Anemia

History: Dec.'44 Weakness and pallor
Mar.'45 Splenomegaly found
Increasing anemia
Numerous transfusions

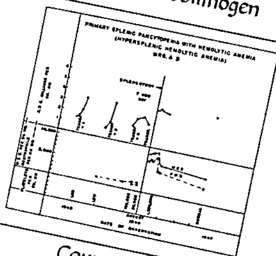
P.E.: Extreme pallor, ? icterus
Liver 4 F.B.; Spleen 6 f.b.

Blood: Hgb. 6.7 Gms.; RBC 2.66 M
WBC 1900; P 75% (1400)
Plts. 160,000
Retics. 2.8%
Bilirubin 1.8 mgs.
Marrow: Hyperplasia
Maturation Arrest of RBC
Fecal Urobilinogen: 307 mgs.
(5x normal)
Splenectomy - 750 Gms. Hyperplasia
Eruthrophagocytosis

NOTE: Only real evidence of hemolytic anemia is high fecal urobilinogen



Note arrested Maturation of Nucleated Red Cells at Erythrogone Level



Course

DATA: (1) Anemia + (2) Idiopathic Splenomegaly + (3) Cytopenias + (4) Increased Hemolysis + (5) Splenectomy → (6) Normal blood

CONCLUSION: Idiopathic Splenomegaly → Pancytopenia (Marrow Inhibition, Maturation arrest) + Increased Hemolysis (Erythrophagocytosis)

SPLENIC PANCYTOPENIA

The Anemia of Splenic Pancytopenia is not always hemolytic

ISABELLE M. AGE 47 - Primary Splenic Pancytopenia, Non-Hemolytic Anemia

History: Oct.'40 Fatigue; Rx Liver
Aug.'42 Menorrhagia
Blood: Hgb. 4.5 Gm. RBC 3.5M.
WBC 3100; Plts. 207,000
X-rays: Splenomegaly (spleen not felt)
Rx. Fe; Liver extract
Hysterectomy
Sept.'45 Ecchymoses
P.E.: Splenomegaly 2 f.b.
Petechiae, ecchymoses

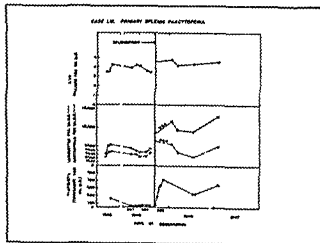
Blood: Hgb. 12.0 Gm; RBC 3.8 M.
WBC 4500; P 70% (3150)
Plts. 35,000
Retics. 1.2 %
Bilirubin 0.4 mgs.
Marrow: Hyperplasia
Megas. inc'd; platelet production dimished
Splenectomy: 430 Gms.
Non-specific hyperplasia

DATA:

(1) Splenomegaly +
(2) Pancytopenia +
(3) Hyperplastic Marrow +
(4) Splenectomy ⟶
(5) Normal Blood Counts

CONCLUSION:

Idiopathic Splenomegaly → Cytopenias (Marrow Inhibition)



Course

SPLENIC PANCYTOPENIA

Various Splenomegalic States → Pancytopenia

MRS. F.G. AGE 41 Sarcoid Splenomegaly with Pancytopenia

History: weakness
fatigue
anorexia
P.E.: axillary nodes
spleen 6 f.b.
Xrays: slight pulmonary fibrosis
Marrow: normal
Spleen: 3x normal
sarcoidosis

	SPLENECTOMY Before	After
Hgb.	8.0 Gm.	14.0 Gm.
RBC	3.9 M.	4.51 M.
WBC	3100	12,900
Polys.	2200	10,700
Plts.	decreased	normal

CONCLUSION: Sarcoidosis → Splenomegaly → Pancytopenia (Marrow Inhibition)

MRS. G.G. AGE 57 Malarial Splenomegaly with Pancytopenia

History: Born in Greece
'41-weakness
fatigue
ecchymoses
'42-petechiae
weight loss
'44-chills & fever
every 72 hrs.
P.E. Liver 3 f.b.
Spleen 10 f.b.
Axillary nodes

Blood: Hgb. 7.0 Gm.
RBC 3.2 M
WBC 2,400
Polys. 1,500
Plts. 59,000
Marrow: Normal
Spleen Puncture
Plasmodium malariae

CONCLUSION: Chronic malaria → Splenomegaly → Pancytopenia (Marrow Inhibition)

HYPERSPLENISM

ETIOLOGY & PATHOLOGY

Etiologic Factors (28 cases)	
Rheumatoid Arthritis	2
Syphilis	2
Cirrhosis of Liver	2
Gaucher's disease	1
Boeck's sarcoid	1
Malarial splenomegaly	1
Hodgkin's splenomegaly	1
Leukemic splenomegaly	2
Idiopathic	16

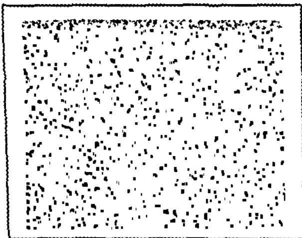
Classification

Primary or Secondary Splenic Cytopenias
- Thrombocytopenia
- Neutropenia
- Neutropenia + Thrombocytopenia
- Pancytopenia
  - with Hemolytic Anemia
  - with Nonhemolytic Anemia

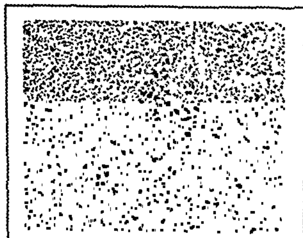
(Other combinations occasionally occur)

PATHOLOGY

Except for those cases of splenomegaly due to known cause
Histology of most cases is unrevealing ("nonspecific hyperplasia")



Spleen: Non-Specific Hyperplasia



Spleen: Erythrophagocytosis

Hypersplenism a functional, not a histopathologic, disturbance

DIAGNOSIS OF HYPERSPLENISM

A Problem in Correct Addition

I

HISTORY

Vague symptoms
Arthralgias
with or without
Anemia
Infections
Bleeding tendency

\+

II

EXAMINATION

Splenomegaly
with or without
Pallor
Icterus
Petechiae & ecchymoses

PLUS

III

BLOOD

Cytopenias
Total: Anemia
Leukopenia
Neutropenia
Thrombocytopenia
or
Selective:
Anemia *or*
Leukopenia
Neutropenia *or*
Thrombocytopenia

\+

IV

BONE MARROW

Normal *or*
Hyperplasia
Total or Selective
with or without
Maturation Arrest
RBC
WBC
Megakaryocytes

If addition is correct, splenectomy successful
Occasionally, one must admit, addition is incorrect

HYPERSPLENISM

A Functional Diagnosis Indicating Splenectomy

RULE OUT

Aleukemic Leukemia

Splenomegaly
Cytopenias
Marrow: Leukemic
Normal (rarely)
Look for:
abnormal blood cells
abnormal marrow

Lymphosarcoma of Spleen

Splenomegaly
Cytopenias
Marrow: Normal or
Hyperplastic or
Infiltrated
Splenic Puncture: Marked lymphoid proliferation
NOTE: Fever, high sedimentation rate

Myeloid Metaplasia of Spleen

Splenomegaly
Cytopenias
Marrow: Hypoplastic
Fibrotic
Look for:
"leukoerythroblastic anemia"
nucleated RBC
myelocytes
low platelets
x-rays: osteosclerosis
hepatomegaly

Siderocytic Anemia

A disorder of Hemoglobin Metabolism

Splenomegaly
Cytopenias
Marrow: Normoblastic Hyperplasia
Look for:
Red Cell Abnormalities
granules in RBC
some nucleated RBC
basophilic stippling
High serum iron

HYPERSPLENISM

Treatment & Prognosis

Medical Therapy - purely symptomatic

- Specific Rx often useful in Malaria, Kala-Azar, Syphilis
- ACTH & Cortisone occasionally effective (Early Felty's)
- Transfusions: of temporary value in anemia
- Penicillin: of value in granulocytopenic sepsis

SPLENECTOMY THE ONLY EFFECTIVE THERAPY IN MOST CASES

- Operative mortality small (< 5%)
- Choose correct surgeon

RESULTS OF SPLENECTOMY (26 CASES)*

Operative Deaths: none

GROUP	Number of Cases	Number Splenectomized	Effect of Splenectomy		
			Cure	Partial Effect	No Effect
Splenic Neutropenia c̄ or s̄ Thrombocytopenia	8	7	6	0	1
Splenic Pancytopenia c̄ Nonhemolytic Anemia	9	8	7	0	1
Splenic Pancytopenia c̄ Hemolytic Anemia	11	11	8	1	2**
TOTALS	28	26	21 (81%)	1 (4%)	4 (15%)

* Does not include idiopathic thrombocytopenic purpura
** Died within 2 months (1) Pulmonary Embolism (2) Hodgkin's Disease

Prognosis: Without splenectomy, slow downhill course
Cure with splenectomy 80%, if diagnosis correct
In secondary cases, underlying disorder unchanged

PATHOGENESIS of HYPERSPLENIC SYNDROMES

THEORIES

SEQUESTRATION" - PHAGOCYTOSIS	MARROW INHIBITION
Spleen captures & Phagocytes large numbers of: RBC → Hemolytic Anemia WBC → Neutropenia Plts. → Idiopathic Thrombocytopenia All 3 → Pancytopenia (Panhematopenia)	Normal Inhibitory Humoral action of Spleen upon Marrow Exaggerated: RBC → Non-Hemolytic Anemia WBC → Neutropenia Megas. → Thrombocytopenia In addition enlarged spleen may destroy too many RBC → Hemolytic Anemia
Pro 1. Beneficial Effect of Splenectomy 2. Erythro - & neutrophagocytosis 3. Results of Adrenalin Test	Pro 1. Beneficial effect of Splenectomy 2. Existence of Non-Hemolytic Anemia 3. Thromb. in newborn infants of thrombocytopenic mothers 4. Effects of splenic extracts → cytopenias 5. Maturation arrest of red cells, granulocytes, megas. in marrow
Con 1. Maturation Arrest in Marrow 2. Absence of Young cells in peripheral blood 3. Absence of Splenic A-V differences 4. Inconstant phagocytosis 5. Adrenalin test often same after Splenectomy	

Weight of Evidence favors Marrow Inhibition by Spleen

PATHOGENESIS of HYPERSPLENIC SYNDROMES

THEORIES

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Weight of Evidence favors Marrow Inhibition by Spleen

PATHOGENESIS OF HYPERSPLENIC STATES

OUR CONCEPTS

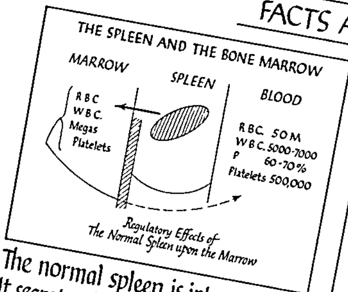
Normally: Splenic Factors act on Bone Marrow to
(1.) Regulate production ± delivery of platelets
(2) Regulate delivery of granulocytes
(3.) Regulate delivery of erythrocytes
Also (4.) Spleen destroys aged red cells

Hypersplenism--An Exaggeration of one or more of these functions

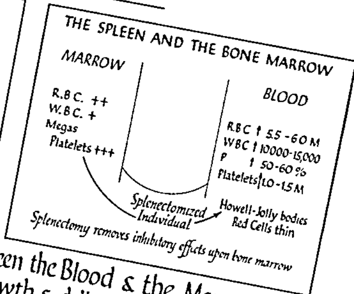
(1) Inhibition of Maturation of Megakaryocytes SPLENIC THROMBOCYTOPENIA *(Idiopathic Thrombocytopenic Purpura)*	(2) Inhibition of Delivery of Granulocytes SPLENIC NEUTROPENIA
(1) + (2) + (3) Inhibition of Production and/or Delivery of R.B.C., Polymorphs., Platelets SPLENIC PANCYTOPENIA with NONHEMOLYTIC ANEMIA	(1) + (2) + (4) Inhibition of Production of Plts. Inhibition of Delivery of Polys. Excessive Destruction of R.B.C. SPLENIC PANCYTOPENIA with HEMOLYTIC ANEMIA

We Believe: (1) Hypersplenism the result of Inhibitory effect(s) of Spleen upon Marrow
(2) Phagocytosis, if present, involves Red cells chiefly
(3) Both mechanisms may be operative in some cases
(4) Delayed or partial response in some cases suggests that spleen may not always be the sole organ concerned
(5) Whatever theory is correct, splenectomy is usually curative

HYPERSPLENISM
FACTS AND FANCIES

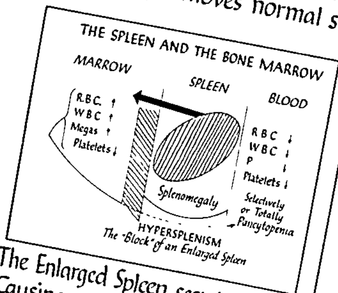


Regulatory Effects of The Normal Spleen upon the Marrow

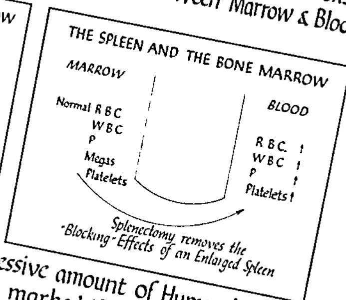


Splenectomy removes inhibitory effects upon bone marrow

The normal spleen is interposed between the Blood & the Marrow
It secretes factors which regulate growth & delivery of marrow cells
Splenectomy removes normal slight "Block" between Marrow & Blood



HYPERSPLENISM
The "Block" of an Enlarged Spleen



Splenectomy removes the "Blocking" Effects of an Enlarged Spleen

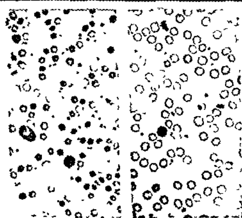
The Enlarged Spleen secretes an excessive amount of Humoral Factors
ausing maturation arrest and a marked "Block"
etween Marrow and Blood
sulting in various types and degrees of Cytopenias

THE SPLEEN AND HEMOLYTIC ANEMIA

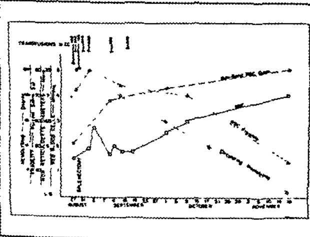
Spleen is at times of central importance in hemolytic anemia.
Micheli & Banti suggested splenectomy in hemolytic anemia
Rationale: Hyperhemolysis by abnormal spleen

CASE L.G. ACUTE HEMOLYTIC ANEMIA

BEFORE SPLENECTOMY	AFTER SPLENECTOMY
Anemia: RBC 1.0 M.	No Anemia: RBC 5.0 M.
Acholuric Icterus	No Icterus
Increased Blood Destruction	Normal Blood Destruction
Spherocytosis; Reticulocytosis	Normal Red Cells
M.C.D. 6.4 Micra	M.C.D. 7.5 Micra
Hypotonic Fragility .72-.44 %	Hypotonic Fragility: .44-.24 %
Serum Hemolysins	No Hemolysins



Blood Picture
Before – Splenectomy – After



Course

BUT Hemolytic Anemia not always a splenic disorder

THE SPLEEN AND HEMOLYTIC ANEMIA

Hemolytic Anemia due to two main mechanisms:

I. An "Intrinsic" defect of the red cells (*Usually Hereditary*)

1. Spherocytosis
2. Leptocytosis (Target-oval cells: Mediterranean Anemia)
3. Drepanocytosis (Target-sickle cells: Sickle cell Anemia
4. Other hereditary defects
5. Acquired Defects
   Pernicious Anemia
   Paroxysmal Nocturnal Hemoglobinuria

II. An "Extrinsic" Factor acting on red cells (Acquired)

1. Parasites (Malaria),
   Bacteria (Streptococcus, B. Welchii, Bartonella)
2. Auto-Immune Antibodies: Agglutinins, Hemolysins
3. Chemicals: Sulfonamides, others
4. Splenomegaly: Hypersplenic Hemolytic Anemia
5. Others

SPLEEN AND HEMOLYTIC ANEMIA

HEREDITARY SPHEROCYTOSIS

Pathogenesis:

a. Inherited (Intrinsic) Defect of Red Cell Formation
b. Activity of Specific Extrinsic Autohemolysin ??
} Spherocytosis

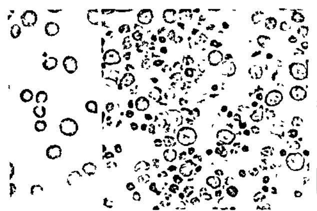
Spherocytosis + Normal Spleen ⟶ Trapping: Increased Hemolysis
Spherocytosis + No Spleen ⟶ No Trapping: Normal Hemolysis

What causes Spherocytosis?

Nucleated red cells normal size
Young red cells (Reticulocytes) normal size
Spherocytosis occurs at last stage of red cell development
Red cell membrane too small for contents

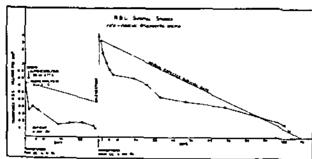
Hemolytic Crisis: The Chief Complication

Findings	These Events Suggest
Sudden, extreme spherocytosis	Exaggeration of usual Hyperhemolysis
WBC, Reticulocytes, Platelets reduced	Extrinsic Hemolytic Factor
Maturation arrest of nucleated red cells	Hypersplenism: Leukopenia
Autohemolysin occasionally found	Reticulocytopenia
	"Maturation Arrest"
	Direct effect on Marrow (Owren)



BLOOD
Spherocytosis,
No Reticulocytosis

MARROW
Maturation Arrest of
Nucleated Red Cells



In crisis: Red Cell survival time diminished
Post splenectomy, survival time normal

SPLEEN AND HEMOLYTIC ANEMIA

ACQUIRED HEMOLYTIC ANEMIA

Due to numerous causes: Chemicals, Parasites, Bacteria,
"Symptomatic," "Idiopathic"

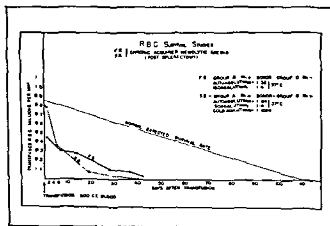
Idiopathic and Symptomatic types usually associated c̄ Abnormal Agglutinins or Hemolysins (Auto-antibodies) in the serum.

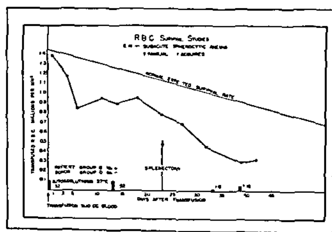
Detection of Antibodies facilitated by:

- Bovine Albumin Solution as serum diluent
- Use of Coombs' Antiglobulim serum
- Use of Trypsinated red cells: Acidification of serum, etc.

Red Cell Survival Time (Ashby Technique): Greatly shortened life span

- Normal transfused red cells disappear quickly
- Indicating an Extrinsic mechanism acting upon R.B.C.





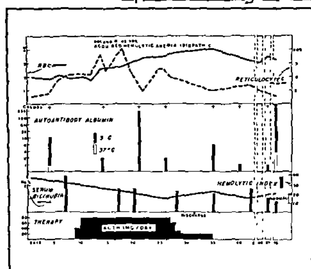
Acquired Hemolytic Anemia (Idiopathic)
Abnormal Iso-antibodies. Diminished Red Cell Survival Time

Splenectomy may fail to control antibody formation

ACTH-CORTISONE THERAPY AND HEMOLYTIC ANEMIAS

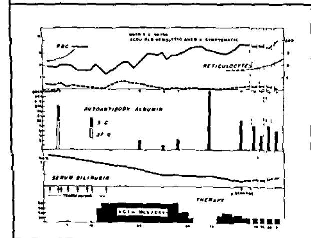
No Value in Hereditary Cases
Valuable in Acquired Cases with Abnormal Antibody
Antibody may occur in both "Idiopathic" and "Symptomatic" cases

Splenectomy often Ineffective



"Idiopathic" Immunohemolytic Anemia
Splenectomy Ineffective

ACTH Rx
Marrow Stimulation
Antibody Reduction with Prolonged Remission



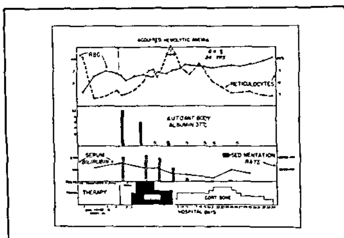
Generalized Lymphosarcomatosis with Immunohemolytic Anemia

ACTH Rx
Antibody Reduction
Hemolysis greatly reduced
Death from Lymphosarcoma

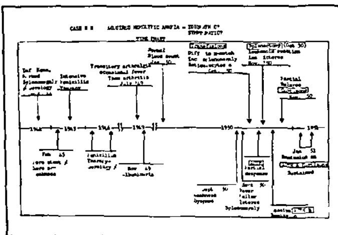
ACTH-Cortisone Therapy will:
a. Reduce Lymphocytic and Splenic Tissue
b. Depress Antibody Formation
c. Reduce Hemolysis
d. Stimulate Bone Marrow

ACTH-CORTISONE THERAPY OF IMMUNO-HEMOLYTIC ANEMIA

Auto-Immunization Develops → Antibody Attacks Patient's Own Red Cells → Shortens Red Cell Life Span → Hemolytic Anemia



"Idiopathic" cases may be part of a broader Syndrome including Periarteritis Nodosa and Disseminated Lupus



Sensitizing Factor

↙ Vascular Allergy (Periarteritis, L.E.)

↘ Immunohemolysis

℞ with ACTH-Cortisone
"Double Target"

↙ Collagen Disturbance

↘ Antibody-producing Tissue

Summary of 22 Cases treated with ACTH-*Cortisone*

1. Remissions in 20 cases
2. Reduction or Disappearance of Antibody
3. Coombs' Test Negative 3 cases
4. Control often possible without Splenectomy
5. Relapsed Splenectomized Cases, with or without Myeloid Metaplasia, strikingly benefited.

SPLENECTOMY IN THE HEMOLYTIC ANEMIAS

HEREDITARY

Spherocytic: (Spleen traps, Destroys Spherocytes)
Splenectomy Curative

Leptocytic (Mediterranean) and Sickle Cell Anemia
Occasional Cases with Marked Splenomegaly, Hemolysis, or Hypersplenic Effects are greatly benefited by Splenectomy

ACQUIRED

Chemical: Transfusions (Splenectomy Contraindicated)

Immunologic: Abnormal Antibody, positive Coombs' test
Try ACTH-Cortisone first
Splenectomy benefits some cases

Primarily of Splenic Origin: with Leukopenia-Thrombocytopenia; Coombs' test Negative
Splenectomy usually Curative

HEMOGLOBINURIAS

Intravascular Hemolysis:
Splenectomy Contraindicated

WHAT SPLENECTOMY DOES

1. Reduces Erythrophagocytosis
2. Stops Splenic Inhibition
3. Removes a source of Abnormal Antibody
4. Removes Spherocyte Trap.

IDIOPATHIC THROMBOCYTOPENIC PURPURA

hemorrhagic disease of unknown cause with marked
latelet reduction often responding dramatically
o splenectomy

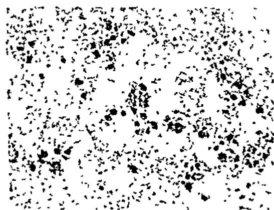
CLINICAL FEATURES

Bleeding -from mucous membranes
-into skin
-into brain

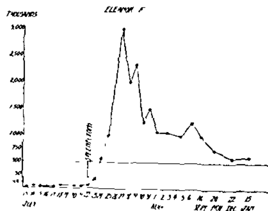
P.E.: Slight pallor
Petechiae & Ecchymoses
Spleen - not felt
Lymphadenopathy - none

TYPICAL BLOOD COUNTS

RBC 4.5 M Hypochromic Anemia
HGB. 70%- 10.8 Gms.
W.B.C. 12,000 Polymorphs. 80%
Platelets 10,000 - 100,000
Bleeding Time +++
Coagulation Time Normal
Clot Retraction Poor
Prothrombin Time Normal



Bone Marrow Hyperplastic
Megakaryocytes +++
Platelet Production ↓↓↓



Splenectomy often results
in great increase
in platelets

"IDIOPATHIC" THROMBOCYTOPENIC PURPURA

Platelets reduced in blood
Bone Marrow Megakaryocytes Normal or Increased
Palpable Spleen unusual

Discriminate between Acute and Chronic Types

ACUTE: No previous history
Affects both sexes
Usually Allergic or Immunologic

[Post-Infectious: 10-14 days after Infection]
[Post-Drug: Sedormid, Quinidine, Sulfa, others]
Persists 1-12 weeks
Complete Spontaneous Recovery
Splenectomy best withheld,
but decision often very difficult

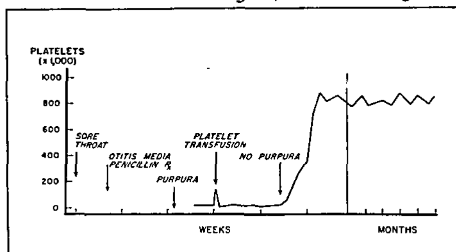
CHRONIC: Usually in females
Long History; Remissions and Relapses
Platelets often large, bizarre
Splenectomy usually successful

GENERAL RULES:
Acute Cases: Leave alone. Transfusions
Chronic Cases: Splenectomy
ACTH-Cortisone: Doubtful Value

"IDIOPATHIC" THROMBOCYTOPENIC PURPURA

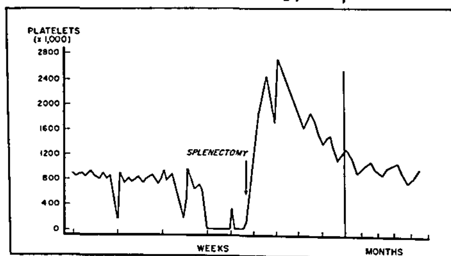
Includes Allergic, Immunologic, Hypersplenic Types

Acute (Allergic, Immunologic)



Sudden Onset; Spontaneous, complete recovery in weeks
℞ : Transfuse; withhold Splenectomy

Chronic (Often Hypersplenic)



Long History; Remissions, Relapses; Platelets always Low
Splenectomy: ℞ of choice

IDIOPATHIC THROMBOCYTOPENIC PURPURA

PATHOGENESIS

Theories:

1. Spleen destroys excessive number of platelets (*Kaznelson; Doan*)
2. Spleen inhibits production of platelets from megakaryocytes: (*Frank; Dameshek*)
3. Immunologic mechanism responsible for platelet destruction: "Immuno-Thrombocytopenia"- (*Evans*)
4. Thrombocytolytic factor in plasma affects platelets and possibly megakaryocytes (*Harrington et al*).

Facts:

1. No evidence of platelet destruction by spleen
   Extirpated spleen studies. In vivo experiments (*Stefanini et al*)
2. Marrow megakaryocytes numerous; little platelet formation
   After splenectomy, platelet formation active (*Dameshek & Miller*)
3. Immunologic mechanism very likely in acute cases.
   Occasional cases, acute and chronic, show platelet agglutinin.
   Immuno-hemolytic anemia and immuno-thrombocytopenia may be present together.
4. Direct transfusion of "Thrombocytopenic" plasma usually causes thrombocytopenia in normals (*Harrington et al*).
   Platelet survival time greatly diminished (*Stefanini et al*)

Conclusions:

ITP may be of heterogeneous origin
- Immunologic
- Humoral (Splenic, other)
- Hypersplenic (Normal spleen, Splenomegaly)
- Phagocytic (Tissues: ?? Spleen)

IDIOPATHIC THROMBOCYTOPENIC PURPURA

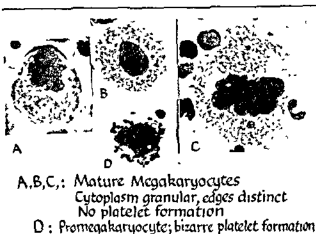
SPLENECTOMY

Kaznelson (1916) introduced Splenectomy "To Reduce Splenic Thrombocytolysis"

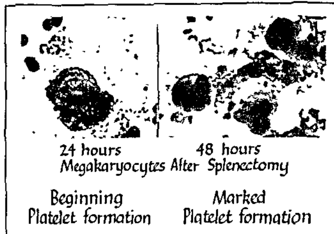
eory may be defective, but operation 60-80% successful in chronic cases

BONE MARROW

Before SPLENECTOMY After



A,B,C,: Mature Megakaryocytes
Cytoplasm granular, edges distinct
No platelet formation
D : Promegakaryocyte; bizarre platelet formation



24 hours 48 hours
Megakaryocytes After Splenectomy

Beginning Platelet formation — Marked Platelet formation

Megas. +++ Platelet Production ---

Megas. +++ Platelet Production +++

Splenectomy removes abnormal hypersplenic organ containing megakaryocyte-inhibiting material.

1872
3869

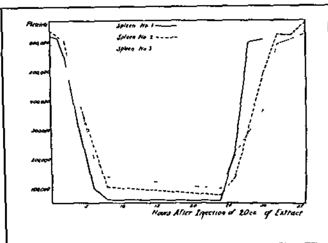
SPLENECTOMY

INDICATIONS	CONTRAINDICATIONS
Platelets low in blood. Megas. high in marrow	Platelets low in blood. Megas. low in Marrow
In Chronic Cases. Preferably done during Remission	In Chemical, Allergic, and Leukemic Thrombocytopenia
In Occasional Acute Cases in Adults, not responding to Transfusions, or ACTH	In Acute Cases, particularly in children

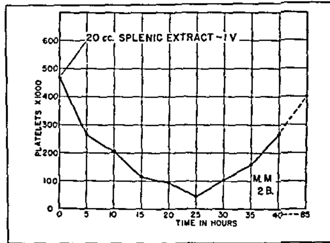
IDIOPATHIC THROMBOCYTOPENIC PURPURA

SPLENIC EXTRACTS

Troland & Lee: Platelet reducing Factor (*"Thrombocytopen"*) present in Splenic Extracts.



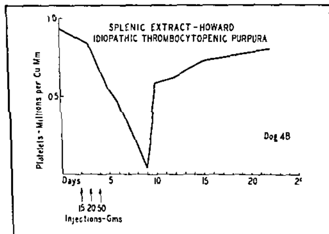
Troland & Lee (1938)



Rose and Bouer (1941)

Effects of Acetone Extracts in Rabbits
Results by other workers inconstant

Our studies: Saline Splenic Extracts in Dogs



Effect of Splenic Extract in Dog



Platelets low in blood. Megas. numerous in mar

Our results suggestive but inconstant; need further study

CONCLUSION: Spleen in Idiopathic Thrombocytopenic Purpura may contain platelet-reducing substance in some cases

CAUSES of SPLENOMEGALY

I. Infectious States

Acute: Typhoid, malaria, infectious mononucleosis*, measles
Subacute: Brucellosis, malaria, bacterial endocarditis*, abscess*
Chronic: Malaria, syphilis, T.B., Kala-azar
Related Disorders: Rheumatoid arthritis, Boeck's sarcoid
Disseminated lupus
Post-Infectious: Amyloidosis

II. Portal & Splenic Vein Hypertension (Congestive Splenomegaly)

Cirrhosis of liver, Portal vein thrombosis
Thrombosis of splenic vein, Other rare causes

III. Excessive Cellular Proliferation*

1. Leukemias: Acute & chronic, leukemic & leukopenic
2. "Lymphomas": Hodgkin's disease, lymphosarcoma, etc.
3. Polycythemia vera
4. Myeloid metaplasia of spleen (with myelofibrosis)

IV. Excessive RBC Destruction: Hemolytic Anemias*

[illegible] Target-Sickle; others
Acquired: Numerous types, including symptomatic.
Hemoglobinurias

V. Disorders of Lipid Cellular Metabolism

Gaucher's Dis[illegible]ase
Xanthomatoses; related disorders

VI. Primary Tumors* and Cysts of Spleen

VII. Idiopathic Types - many cases, ? post-infectious

[illegible]

* *Usually with leukocytosis*

DEMONSTRATION of SPLENOMEGALY

THE ENLARGED SPLEEN IS TOO OFTEN MISSED

Inspection

Very large spleen causes left upper abdominal bulge
Chronic splenomegaly in the young causes bulge left lower chest wall

Palpation

Patient on back : High flat table; patient breathes naturally
Stand at right of patient
Left hand behind ribs; right hand rests gently on left abdomen
Spleen moves down with inspiration; hits fingers
Patient on right side: Often helpful to bring out slight splenomegaly
Patient sitting or standing: Sometimes helpful

Percussion

Do routinely: Normal dullness: 7th to 9th ribs, anterior & midaxillary lines
Splenomegaly: Dullness to costal margin or below

Auscultation

Friction rub: In splenic infarction, perisplenitis
Bruit: Rare: splenic aneurysm, pressure on splenic artery

Xrays

Careful flat plates of abdomen demonstrate splenomegaly
Xrays of stomach, bowel, kidneys may be of value:
(displacement; pressure)
Thorotrast visualization rarely necessary

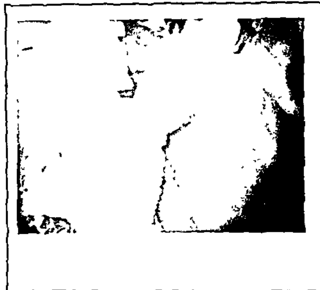
X-RAY VISUALIZATION

Careful X-rays usually give good splenic visualization

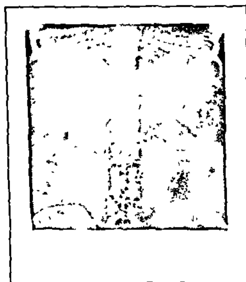
Technique: Flat plate of Abdomen with Bucky Diaphragm



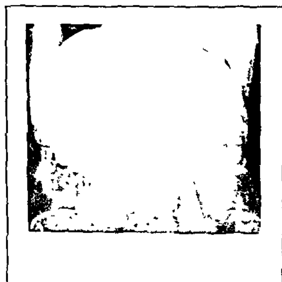
Normal Spleen Often Visualized



Moderate Splenomegaly-Pressure on Stomach



Moderate Splenomegaly (T.B.) Kidney Displacement

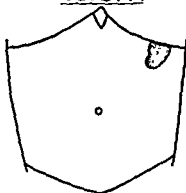


Marked Splenomegaly

X-rays Often Demonstrate Unsuspected Splenomegaly

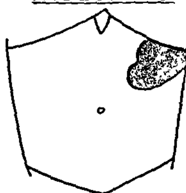
SHORT CUTS IN THE DIAGNOSIS OF SPLENOMEGALY

SLIGHT



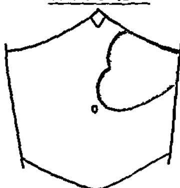
Acute, subacute infections
Pernicious Anemia, at times
Acute Hemolytic Anemia
Acute Leukemia

MODERATE



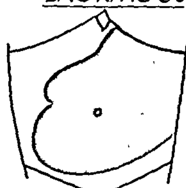
Subacute Infections
Boeck's Sarcoid
Portal Hypertension
Gaucher's Disease
Chronic Hemolytic Anemia
Chronic Lymphocytic Leukemia
Lymphoma

MARKED



Polycythemia Vera
Gaucher's Disease
Tumors
Chronic Granulocytic Leukemia
Myeloid Metaplasia

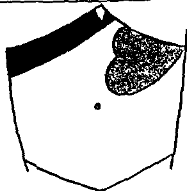
ENORMOUS



Chronic Granulocytic Leukemia
Kala-Azar
Hodgkin's (occasionally)
Cysts
Gaucher's disease

SHORT CUTS IN THE DIAGNOSIS OF SPLENOMEGALY

Spleen and Liver



Granulocytic (Myelogenous) Leukemia
Cirrhosis of Liver
Chronic Leukemia
Syphilitic Hepato-Splenomegaly
Gaucher's Disease
Polycythemia Vera
Hemolytic Anemia
Extramedullary Hematopoiesis

Spleen & Bone Disease

1. Gaucher's Disease
2. Hand-Schüller-Christian
3. Osteosclerosis
4. Multiple Myeloma *(rare)*
5. Lymphoma *(occasional)*

Spleen & Pigmentation of Legs

Gaucher's Disease
Sickle Cell Disease *(rare)*
Siderocytic Anemia *(rare)*

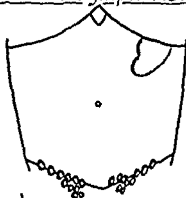
Spleen and Jaundice

1. Slight Icterus
   Hemolytic Anemias
   Hepatic Disease
2. Marked Icterus
   Hepatic Disease

Spleen and Pallor

1. with Icterus: Hemolytic Anemia
2. without Icterus: Leukemias
   Lymphomas
   Hypersplenic anemia

Spleen and Lymph Nodes



Lymphocytic Leukemia
Lymphomas, including
Hodgkin's, Lymphosarcoma, Giant Follicle Lymphoma
Sarcoidosis

STUDY OF A CASE OF SPLENOMEGALY

I. History: Racial Origin*. Mediterranean, African, Jewish (Gauchers)
Familial: Hemolytic anemias; Gaucher's; others
Chemical Exposure: Alcohol, Benzol, Drugs
Infections: Tropical disease, malaria, syphilis, etc.
Recent Infections: ? Neutropenia
Recent bleeding: ? Thrombocytopenia

II. Examination: Pallor, icterus, petechiae, ecchymoses
Hepatomegaly, "spiders," venous distension
Lymphadenopathy
Skin eruptions, pigmentation
Bone and joint disturbances

III. Laboratory Data

A. Blood:
*Hgb., RBC, WBC, Differential,
*Platelets, reticulocytes, character of red cells
*Bilirubin, fragility tests
Serologic tests (Wasserman, etc)

B.* Marrow:
Sternal puncture - most cases
Trephine biopsy - occasionally

C. Urine:
Bilirubin, urobilinogen, Bence-Jones

D. Stools:
*Urobilinogen output (? Hemolysis)

E. X-rays:
Chest
*Abdomen - spleen size
Esophagus - ? varices
G.I. Series, G.U. series at times
Bones: Sclerosis, Gaucher's, etc.

F. Special Procedures:
Lymph Node biopsy
Liver biopsy
Splenic puncture; splenic biopsy
Adrenalin Test **
Xray treatment over spleen
Intravenous thorotrast
Splenectomy in some cases

*Most important
**Adrenalin Test: Not helpful in our hands

Critique. Adrenalin acts on Nodes, Marrow, Liver as well as on spleen
Similar results pre- and post-splenectomy
Mechanism of Results Uncertain

STUDY OF A CASE OF SPLENOMEGALY

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MYELOID METAPLASIA OF THE SPLEEN

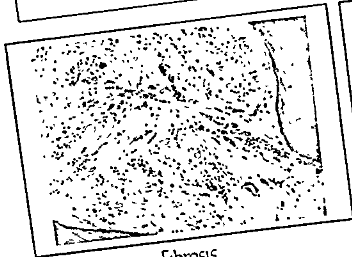
An Important Diagnostic Problem

I. Bone Marrow becomes sclerotic
because of
Overactivity (polycythemia)
Destruction (chemicals, Xrays)
Unknown causes

II. R-E. Tissue Assumes
Fetal Hematopoietic Functions
In: Lymph Nodes
: Liver
: Spleen

III. Results
Extramedullary Hematopoiesis
("Myeloid Metaplasia") in
Spleen, to large extent
Liver, somewhat
Lymph nodes, slight
- Splenic blood formation insufficient
- Splenic auto-regulation inefficient

Blood shows anemia
early red cells
WBC 15,000 to 30,000
Thrombocytopenia



Marrow: Fibrosis



Spleen: Myeloid Metaplasia

Diagnosis: (1) Osteosclerosis (Xrays) + (2) Splenomegaly +
(3) Leuko-Erythroblastic Anemia + (4) Sclerotic Marrow (biopsy)

Splenectomy Contra-Indicated: It removes chief organ
of blood formation

SPLENIC PUNCTURE

An Important Diagnostic Test in Splenomegaly

Indications:

Undiagnosed Splenomegaly with:
- Essentially Normal Blood Picture
- "Dry" Marrow Punctures
- ? Myeloid Metaplasia

Contraindications: Hemorrhagic Disease: Marked Thrombocytopenia

Technique:
- Use 20 gauge needle attached to syringe
- Patient Inspires deeply and holds breath
- Quick Subcostal Intrasplenic Puncture
- Quick Strong Aspiration
- Aspirate Ejected: Smears made, stained

SPLENIC SMEARS



NORMAL



MYELOID METAPLASIA



CHRONIC GRANULOCYTIC LEUKEMIA



LYMPHOSARCOMA OF SPLEEN

SPLENECTOMY

INDICATIONS AND CONTRAINDICATIONS

INDICATIONS

I. Absolute and Urgent: Splenic Rupture,
Traumatic and Spontaneous

II. Urgent: Hemolytic Crisis (Rarely)
Idiopathic Thrombo. Purpura (Rarely)

III. Essential: Idiopathic Thromb. Purpura, most chronic cases
- Hereditary Spherocytosis
- Acquired Hemolytic Anemia –
  Some cases (Try ACTH first)
- Hypersplenic Neutropenia, Pancytopenia, Idiopathic
- Hypersplenism secondary to known benign causes:
  - Rheumatoid Arthritis; Gaucher's Disease, etc.
  - Splenic Cysts, Tumors and Abscesses

IV. Possibly Valuable:
- Certain Mediterranean and Sickle Cell Anemias with excessive Hemolysis
- Certain cases of Leukemia & Lymphoma with Hemolytic Anemia
- Congenital Hypoplastic Anemia (Selected Cases)
- Bulky Spleen interfering with motion

CONTRAINDICATIONS:

I. Absolute: Sclerosis of Marrow c̄ Myeloid Metaplasia of Spleen

II. Definite: Leukemias, Lymphomas (*great bulk of cases*)

III. Fairly Definite: Mediterranean & Sickle Cell Anemia (*most cases*
- Paroxysmal Nocturnal Hemoglobinuria
- Subacute Bacterial Endocarditis
- Malaria, Kala-azar

PREPARATION FOR SPLENECTOMY

I. Emergency Splenectomy, Rarely Indicated
  (Excepting for Splenic Rupture)

II. Preoperative Preparation
  - Correct Anemia
  - Reduce Hemorrhagic Tendency
  - Prevent and Control Infection

III. Blood Transfusions in Hemolytic Anemia
  - Transfuse cautiously, especially in crisis
  - Fresh blood desirable; washed Red Cells often valuable
  - Careful cross-matching of blood
    (special antibody techniques often desirable)
  - Determine basis of reactions:
    ? Isosensitization, ? Plasma Reaction

IV. Blood Transfusions in Thrombocytopenic Purpura
  - Fresh, platelet-rich blood advisable
  - Polycythemic blood desirable

V. ACTH or Cortisone Therapy
  - Reduces transfusion requirement in Acquired Hemolytic Anemi
  - May reduce hemorrhagic tendency in Acute Purpura

VI. Preoperative Antibiotic Therapy
  - Desirable in all cases
  - Especially indicated in presence of Leukopenia

VII. Gastric Decompression by Inlying Tube
  - An Aid to Splenectomy in Most Cases
  - Contraindicated in Purpura; may cause bleeding

ANESTHESIA FOR SPLENECTOMY

I. GENERAL ANESTHESIA PREFERRED EXCEPT IN CASES OF PURPURA

Endotracheal Technique with Controlled or Assisted Respiration
- Provides motionless diaphragm; quiet viscera

Cyclopropane and Curare Preferred Agents
- Provide optimum muscular relaxation
- minimum circulatory depression

Avoid Spinal Anesthesia in Hemolytic Anemia
- May produce circulatory depression

II. SPINAL ANESTHESIA PREFERRED IN THROMBOCYTOPENIC PURPURA

Low Spinal (T_7) Single Dose Technique

Pontocaine and 10% Dextrose Preferred Agents

Supplementary Inhalation Anesthesia:
- Cyclopropane or Nitrous Oxide

Avoid Trauma and Bleeding in Thrombocytopenic Purpura
- Do not use: Endotracheal Tubes, Gastric Tubes, Metal Airways, Continuous Catheter Spinal Anesthesia

III. USE SMALL DOSES OF PREOPERATIVE MEDICATION FOR PATIENTS WITH ANEMIA

SPLENECTOMY: CONVENTIONAL TRANSABDOMINAL TECHNIQ

I. Indications: Most Cases

Advantages: Good Abdominal Exposure

II. Incision

Left Rectus Muscle Splitting Extended to Costoxiphoid Juncti

III. Abdominal Exploration

Always Advisable as First Procedure, except in Purpura

Look for: Associated or Etiologic lesions

- Accessory Spleen
- Cholelithiasis (Hemolytic Anemias)

IV. Mobilization of Spleen

1. Sever superiolateral attachments
   - Peritoneal reflection
   - Splenorenal ligament
2. *Deliver Spleen outside abdomen, if possible*
3. Detach Spleen from Stomach and Colon
   - Gastrosplenic Ligament containing Vasa Brevia
   - Small Portion of Gastrocolic ligament

V. Splenic Pedicle

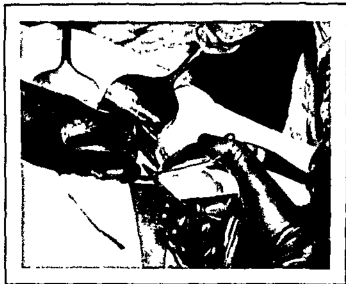
1. Ligate splenic artery
2. Ligate splenic vein
3. Detach tail of pancreas from hilus

VI. Re-explore for Accessory Spleen

VII. [illegible]

Drainage Unnecessary

MOBILIZATION OF SPLEEN
CONVENTIONAL TRANSABDOMINAL SPLENECTOMY



With left hand, pull spleen downward and medially. Expose lateral abdominal gutter



Sever relatively avascular peritoneum and splenorenal ligaments laterally. Exteriorize the spleen

MOBILIZATION OF SPLEEN
CONVENTIONAL TRANSABDOMINAL SPLENECTOMY



(Spleen now resting on left side of abdominal wall). Begin medial mobilization by severing portion of gastrocolic omentum



Sever gastrosplenic ligament containing vasa brevia. Accurate hemostasis essential.
Avoid injury to the stomach

EXCISION OF SPLEEN
CONVENTIONAL TRANSABDOMINAL SPLENECTOM



Gastrosplenic ligament has been severed, exposing hilus attached to pancreas. Splenic artery and vein course along superior border



Splenic artery ligated first, then vein. Tail of pancreas then separated from hilus

EXCISION OF SPLEEN
CONVENTIONAL TRANSABDOMINAL SPLENECTOMY



Photograph of Accessory Spleen removed 15 years after splenectomy. Search *carefully* for accessory spleens and remove if present



Secure hemostasis of pancreas and splenic bed by peritonealizing area. Close abdominal wound without drainage

SPLENECTOMY IN BLOOD DYSCRASIAS

IMPORTANCE OF ABDOMINAL EXPLORATION

I. Associated Lesions often Etiologic in Secondary Hypersplenism
- Portal Bed Blocks: Extrahepatic Lesions; Cirrhosis of Liver
- Abdominal Tumors: Sometimes Related to Splenic Hyperfunction

II. Cholelithiasis Found in Most Patients with Hemolytic Anemia
- Cholelithiasis in Hereditary Spherocytosis 75%
- Simultaneous Splenectomy and Cholecystectomy usually possible

III. Find and Remove Accessory Splenic Tissue
- Otherwise Recurrence of Hereditary Spherocytosis and Thrombocytopenic Purpura possible

IV. Incidence of Accessory Spleens as found at operation

Idiopathic Thrombocytopenic Purpura	20%
Hereditary Spherocytosis	33%
Children	60%
Multiple Accessory Spleens	21%
Total Incidence Accessory Spleens All Cases	28%

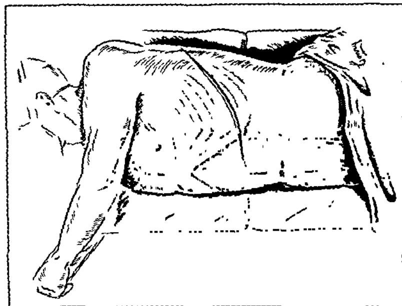
V. Sites of Accessory Spleens
- Hilus and Pedicle (*Most common*)
- Retroperitoneum in Region Pancreas, Kidney, Left Colon
- Omentum, Particularly Gastrocolic Omentum
- Splenic Ligaments: Splenorenal, Gastrosplenic
- Mesentery: Large and Small Intestine
- Gonads (*Rare*)

TWO IMPORTANT MODIFICATIONS OF SPLENECTOMY

I. Abdominothoracic Incision - Improves Exposure
II. Preliminary Ligation of Splenic Artery - Decreases Bleeding

Indications for either or both maneuvers

1. Very Large Spleen
2. Adherent Spleen with Vascular Adhesions
3. Splenectomy with Splenorenal Anastomosis

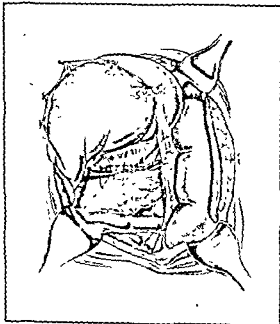


TECHNIQUE ABDOMINOTHORACIC INCISION

Place patient at 45° angle, left side up. Make oblique incision across left rectus extending into 9th intercostal space opening thorax. Incise diaphragm and spread ribs.

TECHNIQUE OF PRELIMINARY LIGATION OF SPLENIC ARTERY

Open gastrocolic ligament and expose splenic artery in lesser omental sac.
Ligate artery along superior border pancreas.



SPLENECTOMY IN LEUKEMIA-LEUKOSARCOMA

INDICATIONS for POSSIBLE SPLENECTOMY:

1. Hemolytic Anemia with Leukemia - Leukosarcoma
   But try ACTH first
2. Primary { Lymphosarcoma / Giant Follicle Lymphoma / Hodgkin's Disease / Reticulum Cell Sarcoma } of the Spleen
3. Cases with Marked Hypersplenic Cytopenic Effects
4. Marked Splenic Sequestration
   Blood "Disappears" in Spleen
   Many Transfusions necessary
5. Spleen so bulky "Life not worth living"

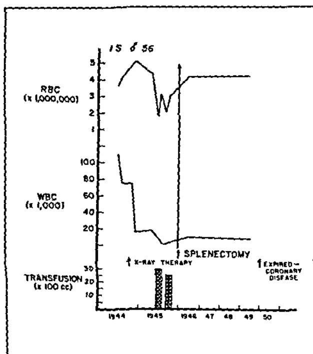
BEFORE SPLENECTOMY

1. Consider Pros and Cons Seriously
   Operative Risk; Transfusion Requirements; Possible Life Span
2. Assay Bone Marrow Situation Carefully:
   1. Megakaryocytes } Should be *present* in fair numbers
   2. Nucleated Red Cells } Should be *present* in fair numbers

RESULTS OF SPLENECTOMY VARIABLE

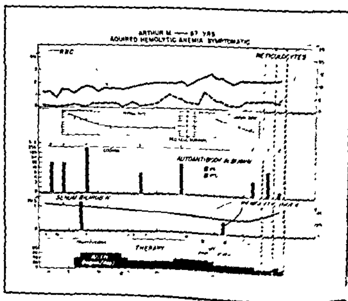
Some Cases greatly benefited; others unaffected
Certain Leukopenic Cases may become frankly Leukemic

SPLENECTOMY IN LEUKEMIA-LEUKOSARCOMA

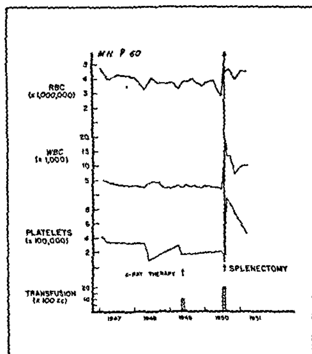


Splenectomy may produce a prolonged Remission in Chronic Lymphocytic Leukemia with Hemolytic Anemia

ACTH-Cortisone caused Reduction in Hemolysis in Lymphocytic Leukemia.
Later, Splenectomy improved Hypersplenic Component



SPLENECTOMY IN LEUKEMIA-LEUKOSARCOMA

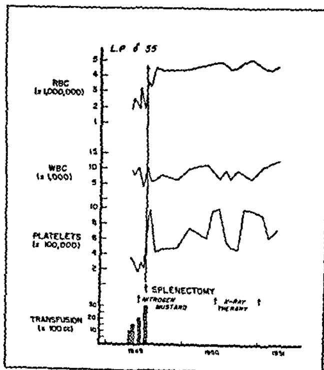


Primary Lymphosarcoma of Spleen may cause Hypersplenism with Pancytopenia

Splenectomy may be strikingly effective

Primary Lymphosarcoma of Bowel resulted in Hemolytic Anemia

Removal of Tumor (plus Splenectomy) curative



RESULTS OF SPLENECTOMY IN 218 CASES OF BLOOD DYSCRASIAS

	NUMBER	GOOD RESULTS
[illegible]		
[illegible]cytosis	38	100%
Acquired Hemolytic Anemia		
Primary	34	50%
Secondary	18	33%
[illegible]penias		
[illegible] Purpura	92	61-80%
Splenic Pancytopenia and Neutropenia		
Primary	20	81%
Secondary	14	71%

MORBIDITY AND MORTALITY

I. Postoperative Complications — All Cases — 22%

II. Minor Complications — 11%

- Wound Complications (Hematoma, Minor Infections)
- Thrombophlebitis (Extremities)
- Atalectasis
- Pleural Effusion
- Subdiaphragmatic Abscess

III. Major Complications

- Lack of Platelet Response in Thrombocytopenic Purpura
  - Gastrointestinal Hemorrhage
  - Cerebral Hemorrhage
  - Bleeding at Operative Site
- Mesenteric Thrombosis
- Continued Hemolytic Tendency in Acquired Hemolytic Anemia

IV. Hospital Mortality — All Cases — 6%

PORTAL HYPERTENSION

I. A Complication of Obstruction in the Portal Venous Bed

Intrahepatic (90%): Cirrhosis of Liver

Extrahepatic (10%): Portal Vein Block (*Congenital or Acquired*)

Normal Portal Venous Pressure: 100-200 mm. H_2O

Portal Hypertension: 300-600 mm. H_2O

II. Sequelae

Esophageal Varices with or without Hemorrhagic Episodes

Splenomegaly - congestive

Hypersplenism usually with Cytopenias

III. Treatment

During Bleeding from Varices

Supportive: Blood Transfusions to replace blood loss

Esophageal Tamponade: Compress bleeding varices

Operative Ligation: Occasionally indicated

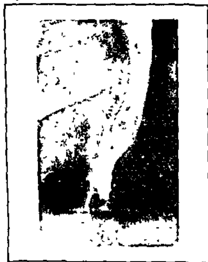
Between Bleeding Episodes

Portal-Systemic Venous Shunts: Best Results

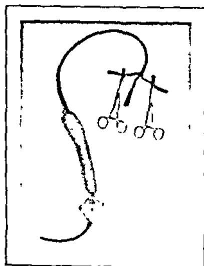
Esophagogastrectomy: Of value in selected cases

Endoscopic Injection of Varices: May be useful

Ligation of Hepatic Artery: On trial



Esophogram showing extensive varices in a patient with portal hypertension



Blakemore-Sengstaken esophageal tamponade tube to compress varices during bleeding The circular balloon is placed in the stomach

PORTAL SYSTEMIC VENOUS SHUNTS FOR PORTAL HYPERTENSION

I. Portal Systemic Venous Shunts Reduce Portal Pressure and Decrease Incidence of Hemorrhage
- Portacaval Shunt effects greatest decompression
  - Preferred Operation in most cases with Cirrhosis of the Liver
- Splenorenal Shunt with Splenectomy: *second best shunt*
  - Necessary shunt in most cases of extrahepatic obstruction
  - Can be used for both intrahepatic and extrahepatic blocks
  - More conservative; portacaval can be done later
  - Probably preferable shunt with marked splenomegaly
  - Tendency to thrombosis greater than with Portacaval Shunt

II. Contraindications to Portal Systemic Venous Shunts
- Severe Liver Disease, unimproved by medical treatment
- Marked Persistent Ascites or Jaundice

III. Preoperative Treatment in Patients with Cirrhosis of the Liver
- Improve Liver Function by Medical Measures
  - Serum Albumin - raise to 3.0 gms. or over
  - Bromsulphthalein Retention - reduce to 30% if possible
  - Ascites should be relieved before operation

IV. Results of Portal Systemic Venous Shunts

Operative Mortality	30 cases	16%
Recurrence of Bleeding Varices	30 cases	10%
(6 months to 4 year follow-up)		

TECHNIQUE OF SPLENORENAL VENOUS ANASTOMOSIS

I. Anesthesia: Endotracheal

II. Left Abdominothoracic Incision Facilitates Exposure

III. Mobilization of Spleen
- Conventional mobilization often possible
- *Ligate splenic artery first - with marked splenomegaly or abundant vascular adhesions*

IV. Dissection of Splenic Vein
- Ligate Splenic Artery before dissecting Vein
- Identify Splenic Vein before detaching Spleen
- Dissect Splenic Vein from groove in superior border of Pancreas
  - Ligate its many small pancreatic branches
- Dissect 5 to 8 cm. of Splenic Vein. Careful hemostasis essential.

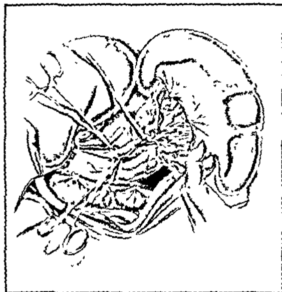
V. End-to-Side Splenic-Renal Vein Anastomosis
- Mobilize Left Kidney
- Occlude Renal Artery and Vein
  - 30 minutes usual period of occlusion
  - Renal Ischemia over one hour undesirable
- Anastomose end of Splenic Vein to Side of Renal Vein
- Reëstablish renal circulation

[illegible]

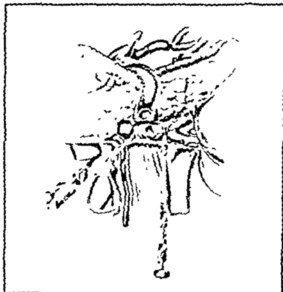
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- Drain thoracic cavity 48 hours

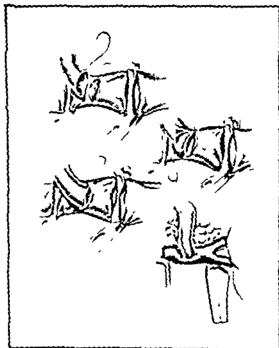
IMPORTANT STEPS IN SPLENORENAL ANASTOMOSIS



Dissection of splenic vein from pancreas. *Ligate carefully small venous branches*



Blalock clamps used to occlude renal vein. Bulldog clamps on renal artery and splenic vein



Detail of Splenorenal Suture Anastomosis:
One row of continuous everting mattress suture used (OOOOO silk); Gauze pressure controls small leaks.
Additional interrupted sutures seldom needed.

PORTAL SYSTEMIC VENOUS SHUNTS FOR PORTAL HYPERTENSION



Exposure of spleen using left-sided abdominothoracic incision for splenorenal shunt



Completed end-to-side splenorenal anastomosis with preservation of kidney.
Portal pressure reduced by 250 mmg. H_2O

TECHNIQUE OF PORTACAVAL ANASTOMOSIS

[illegible]

Dissect Entire Portal Vein

V. End-to-[illegible]

Occl[illegible]

Ligate Portal Vein close to Liver

Secure longest possible segment of Portal Vein to avoid tension

Mobilize Vena Cava from Renal Veins to inferior border of Liver

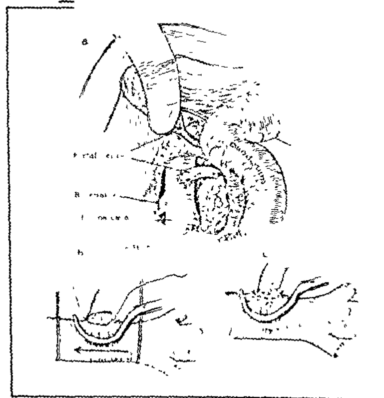
Occlude Vena Cava partially with Non-crushing Forceps

Perform anastomosis without obstructing caval flow

Do not obstruct Renal Veins; Severe kidney damage with anuria may result

VI. Side-[illegible]

W[illegible]



a) Complete suture portacaval anastomosis

b) Anastomosis of end of portal vein to side of vena cava above renal vein entrances; Thomas Smith clamp in place. Note free caval flow beneath clamp.

c) Anastomosis completed. Note everting type of suture

VII. Closure and Drainage of Thorax as in Splenorenal Anastomosis

PORTAL SYSTEMIC VENOUS SHUNTS FOR PORTAL HYPERTENSION



Completed end-to-side portacaval anastomosis performed above renal veins. Portal pressure reduced by 300 mms. of H_2O



Completed side-to-side portacaval anastomosis. Portal pressure reduced by 200 mms. H_2O

SUMMARY & CONCLUSIONS

I. The Spleen has Many Functions, relating chiefly to the Marrow and Blood Cells

II. Chief Splenic Functions:

[illegible]

RBC WBC Plts.	Production and Delivery	B. Reservoir Erythrostasis C. Phagocytosis

III. The Normal Spleen is not essential for life

IV. [illegible]

V. It is important to recognize Abnormal Splenic Syndromes

VI. Hypersplenism: the result of Abnormal Excessive splenic activity

: "Primary and Secondary types } occur
: "Selective" and "Total" Cytopenias } occur
: Splenomegaly almost always present, except in Idiopathic Thromb. Purpura
: Diagnosis:
Cytopenias, splenomegaly,
cellular (non-leukemic) marrow
: Therapy: Splenectomy usually curative.

VII. Continued Studies, Clinical, Experimental [illegible]

[illegible]

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